REMARKS

Favorable reconsideration of the subject application is respectfully requested in view of the following remarks. Prior to entry of this Amendment, claims 1-29 and 31-57 are pending, and claims 1-14, 36-46, 53, 54, 56, and 57 are under consideration. Applicants thank the Examiner for acknowledging the addition of claims 56 and 57. By the present Amendment, claims 4, 8, 15-29, 31-35, 47-52 and 55 are canceled, and claims 2, 9 and 10 have been amended to more specifically describe certain aspects of the invention and maintain proper dependency. It is urged that support for these amendments is provided throughout the specification and claims as originally filed and does not, therefore, constitute new matter. Furthermore, this Amendment is not to be construed as acquiescence to any rejection and is made without prejudice to prosecution of any subject matter modified by the Amendment in a related divisional, continuation, or continuation-in-part application.

Rejection Under 35 U.S.C. § 112, First Paragraph

Claim 57 stands rejected under 35 U.S.C. § 112, first paragraph, for allegedly containing new subject matter that was not described in the specification in such a way as to reasonably convey to the skilled artisan that the inventors had possession of the claimed subject matter at the time the application was filed. Specifically, the Action asserts that the recitation of antibodies or antibody parts bound to an array covalently or by first binding protein G to the array is not disclosed in the instant specification.

Applicants respectfully traverse this basis of rejection and submit that the claimed invention is described in the instant specification in sufficient detail such that the skilled artisan would appreciate that Applicants had possession of the invention as claimed. Specifically, Applicants submit that support for covalent binding of antibodies or antibody parts to the array is provided at page 27, lines 1-2. In addition, support for antibodies or antibody parts being bound to the array by first binding protein G to the array is clearly provided in Example 1, at page 50, lines 11-18. Thus, Applicants submit that claim 57 is fully supported by the instant specification and does not constitute new matter, and respectfully request that this basis of rejection be withdrawn.

Rejection Under 35 U.S.C. § 112, Second Paragraph

Claims 4 and 8 stand rejected under 35 U.S.C. § 112, second paragraph, for allegedly being indefinite in their recitation of arrays of specific formulas to describe arrays of the invention. Specifically, the Action asserts that it is unclear whether the array is a mathematical representation of a rectangular arrangement of quantities, or a substrate for detecting biological interactions.

Without acquiescence to this basis of rejection and solely to expedite prosecution of the instant application, claims 4 and 8 are canceled, thereby obviating the basis of this rejection. Applicants respectfully request that this rejection be withdrawn.

Rejection Under 35 U.S.C. § 102(b)

Claims 1-4, 6-8, 14, 36-42 and 45 stand rejected for allegedly being anticipated by Clackson *et al.* Specifically, the Action asserts that Clackson *et al.* discloses an ELISA device comprising a combinatorial library of rearranged heavy and light chains arranged in a matrix, wherein binding is judged by a variable signal and is indicative of a condition.

Applicants respectfully traverse this basis of rejection and submit that the claimed invention is not anticipated by Clackson *et al.* As an initial matter, Applicants note that claims 4 and 8 are canceled without acquiescence to this basis of rejection. Regarding the remaining claims, Applicants submit that Clackson *et al.* fails to anticipate these claims, since it fails to teach each element of the claims. As stated in the M.P.E.P, "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). Specifically, Applicants submit that Clackson *et al.* fails to teach an array wherein "the **pattern** of interaction between the molecules and the binding partners" is indicative of a condition or particular binding partner, as presently claimed.

As an initial matter, Applicants submit that the presently claimed invention comprises an array of molecules capable of binding to their respective binding partners in a sample or library, wherein the **pattern of binding** of binding partners in the sample or library to

the arrayed molecules is indicative of a condition or the presence of a particular binding partner. Thus, the claimed array provides a molecular profile defined by binding to multiple different arrayed molecules and, therefore, characterized by the pattern of binding observed at multiple sites on the array. The array of the invention, therefore, provides a means of determining the presence or absence of conditions characterized by differences in specific patterns of binding, based on the presence or absence of binding and/or the relative amount of binding. Accordingly, the invention provides a more sensitive assay for indicating the presence of a condition or binding partner, particularly multi-factorial conditions that are not readily indicated by a change in any single binding interaction. Similarly, the invention, since its read-out is based on patterns of binding for multiple molecules, provides additional advantages in indicating the presence of a particular conditions or binding partners that might be only subtly different from related conditions or binding partners, and, thus might only be determined based upon the examination of multiple binding interaction and the determination of the presence of a specific pattern that is indicative of the condition or binding pattern. One specific example described in the instant specification is immunophenotyping (page 24, lines 14-24). Accordingly, the skilled artisan would clearly recognize that the claimed arrays are novel over previously described arrays that are not configured so as to allow the determination of patterns of interaction.

In contrast, Clackson *et al.* absolutely fails to describe any array wherein a **pattern** of binding interaction is indicative of a condition or binding partner. Applicants strongly disagree with the Examiner's apparent assertion that Clackson *et al.* teaches an arrayed combinatorial library. Rather, Applicants submit that the array described in Clackson *et al.* is used to screen a combinatorial library, but the library itself is not arrayed. Instead, Clackson *et al.* describes a method for screening phage display libraries expressing recombinantly-engineered combinatorial antibodies to identify specific antibody fragments and combinations thereof that bind a particular hapten. Clackson *et al.* describe screening hierarchical libraries on 96-well plates by ELISA, in order to detect individual phage clones (not complex biological samples or libraries) expressing a combinatorial antibody that binds the hapten. According to the experimental methods described in Fig. 2, each 96-well plate was coated with either hapten-BSA or BSA alone. Thus, each well of any individual plate was coated with the same molecule.

Since each well is coated with the same molecule, it would clearly be impossible for any distinguishing binding pattern to exist, *i.e.,* each well would display the exact same binding pattern when exposed to the same sample or library. Accordingly, the arrays allegedly described by Clackson *et al.* do not posses the feature of the presently claimed arrays, namely that the arrayed molecules produce a pattern of interaction that is indicative of a condition or a particular binding partner.

Furthermore, the skilled artisan would clearly understand, based upon the teachings of the specification, that the presently claimed arrays comprise a plurality of different arrayed molecules, and can, therefore, be clearly distinguished from the 96-well plates described by Clackson *et al.* which do not contain a plurality of arrayed molecules, but, rather, as noted above, contain the same molecule in each well. Of course, this is suitable for screening isolated clones, as described in Clackson *et al.,* but would not provide a distinct pattern when screening a sample or library, as provided by the present invention.

In addition, it should be pointed out that the grid provided in Fig. 2 is merely the graphical means the authors elected to represent the results of their experiments and does not represent an actual physical array. Furthermore, each event depicted in the grid is evaluated individually (*i.e.,* the clone is isolated and the Vh or Vk gene sequenced and analyzed), and the pattern as a whole has no meaning and, therefore, is not itself indicative.

In light of these remarks, Applicants submit that Clackson *et al.* fails to teach an array that possesses all features of the claimed device and, therefore, fails to anticipate the instant claims. Applicants respectfully request that this basis of rejection be withdrawn.

Rejection Under 35 U.S.C. § 103

Claims 1-14, 36-46, 53, 54 and 56 stand rejected under 35 U.S.C. § 103(a), as allegedly being unpatentable over Clackson *et al.* taken with Marks *et al.* in view of Gallo *et al.* Specifically, the Action asserts that Clackson *et al.* provides the teachings described above in the context of the Section 102 rejection, but concedes that Clackson *et al.* fails to disclose labeled antibodies as recited in claims 53 and 54 or the further limitations described in claims 5, 9-13 and 43-46. Rather, the Action asserts that Marks *et al.* discloses the use of labeled antibodies,

and Gallo *et al.* describes methods of treatment of cancer using monoclonal antibodies capable of binding cell surface determinants. The Action concludes that the skilled artisan would have been motivated by the improvements of Marks *et al.* to improve on the method of treatment of diseases caused by pathogens as taught by Gallo *et al.* by using antibodies with greater diversity and strong binding as taught by Clark *et al.*

Applicants traverse this basis of rejection and submit that the Action fails to establish a *prima facie* case of obviousness, since the cited references do not teach or suggest each element of the claimed invention, as is clearly required in order to establish a *prima facie* case of obviousness. *In re Royka*, 490 F.2d 981 (CCPA 1974). More specifically, Applicants submit that the subject matter of the instant claims is not obvious in light of Clackson *et al.*, Marks *et al.*, and Gallo *et al.*, either alone or in combination, since none of these references teach the feature that the pattern of interaction between arrayed molecules and their binding partners is indicative of a condition or particular binding partner, as recited in each of the claims. In addition, Applicants note that claims 4 and 8 have been canceled without acquiescence to this basis of rejection.

In addition, Applicants respectfully point out that the present claims are drawn to an assay device comprising an array of molecules, which bind to their cognate binding partners in a sample or library to produce a binding pattern indicative of a particular condition or binding partner. Accordingly, the skilled artisan would appreciate that the claimed invention may be used in the detection of a disease. In contrast, the arguments provided in the Action as allegedly demonstrating obviousness of the claimed invention appear largely directed to methods of treating disease, although the cited references do not appear to necessarily provide such teachings. For example, the Action asserts that Marks *et al.* describes the treatment of bacterial and viral infections with peroxidase labeled antibodies, but the cited passages appear directed to the use of such labeled secondary antibodies in western blots to detect bound primary antibody. Nonetheless, Applicants note that while Marks *et al.* describes the use of labeled secondary antibodies to detect binding (which is admittedly well-known in the art), Marks *et al.* fails to teach or suggest arrays suitable for determining molecular profiles, as provided by the instant

invention. Accordingly, Marks *et al.* fails to remedy this deficiency of Clackson *et al.*, and the combination, therefore, fails to render obvious any of the instant claims.

The Action cites Gallo *et al.* as disclosing a treatment for cancer and immunological disorders, such as in instant claims 5 and 43. However, Applicants note again that that these claims are drawn to an assay device comprising an array of molecules and are not, in fact, drawn to methods of treatment. Furthermore, Applicants submit that these claims also recite the feature that the pattern of interaction between the arrayed molecules and their binding partners in a sample or library is indicative, a feature clearly not described in Gallo *et al.* While Gallo *et al.* describes specific methods of separating out cells of interest using antibodies directed to cell surface markers, Gallo *et al.* makes absolutely no reference to any specific patterns of markers being indicative of a condition.

Clearly, the cited references fail to teach each element of the claimed invention. However, Applicants submit that even assuming *arguendo* that they did, the Action fails to establish any motivation to combine the cited references to achieve the claimed invention. As established by the courts and enunciated in the M.P.E.P., "[o]bviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention when there is some teaching, suggestion, or motivation to do so found either explicitly or implicitly in the references themselves or in the knowledge generally available to one of ordinary skill in the art." M.P.E.P., 8th Ed. § 2143.01. In the present case, none of the references teach, suggest or would motivate the skilled artisan to combine the references to achieve the claimed invention. Contrary to the Actions' stated reasoning, Marks *et al.* is not related to a general method of treatment, and, therefore, there is no basis for the Action's argument that improvements in method of treatment described by Marks *et al.* would be applicable to treatment of disease as described by Gallo *et al.* Accordingly, any rejection relying on this combination of references would appear to rest upon impermissible hindsight based upon the instant application's description of the claimed arrays.

In conclusion, since it is clear that none of the cited references teach or suggest an array wherein the pattern of binding between the arrayed molecules and their binding partners in a sample or library is indicative, Applicants submit that the Action fails to establish a *prima facie*

case of obviousness. Accordingly, Applicants respectfully request that this basis of rejection be withdrawn.

The Director is authorized to charge any additional fees due by way of this Amendment, or credit any overpayment, to our Deposit Account No. 19-1090.

Applicants respectfully submit that all of the claims remaining in the application are now clearly allowable. Favorable consideration and a Notice of Allowance are earnestly solicited.

Respectfully submitted,

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